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MALFORMATIONS FOUND BY AUTOPSY OF CLONED AND TRANSGENIC PIGLETS OF DIFFERENT BREEDS

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Viability of cloned and transgenic piglets is seriously compromised and one obvious reason is malformation of vital organs. The aim of the present study was to describe malformations in dead pre-weaned piglets born after transfer to Large White (LW) recipients of cloned (LW donor cells) or transgenic (Yucatan or Göttingen donor cells) embryos. Donor cells were fibroblasts, and the Göttingen and Yucatan cells were made transgenic with one of 5 genes related to different human diseases. Handmade cloning was used to produce embryos that after 5 to 6 days *in vitro* culture were transferred to 108 LW sows 4 days after natural heat. Of these, 21 sows delivered cloned LW piglets, while 17 and 16 sows delivered transgenic Göttingen and Yucatan piglets, respectively. Stillborn and dead pre-weaned piglets were necropsied and malformations registered. Data were analyzed by Fisher's Exact test with a significance level of $P<0.05$. In the 54 litters, total litter size ranged from 1 to 22 piglets (mean 5.4±0.5), and the overall mortality rate until weaning was 59%. Malformations were found in piglets from 38 litters where in average of 35% of the piglets showed malformations (between 8 and 100%). In those litters, 1-7 piglets had one (n=78), two (n=24) or several (n=5) malformations (Table 1). The malformation rates in the transgenic Göttingen (55%) and Yucatan (44%) were significantly higher than in the cloned LW piglets (13%). Some of the malformations seemed to be related to breed and/or transgene; for instance were heart malformations most frequent in Yucatan litters (70%) independent of the transgene, and gall bladder and gonade malformations were more frequent (76% and 86% respectively) in various litters with the same transgene.

These results show that the use of cloning in pigs results in a considerable loss of piglets due to malformations and use of transgenic cells for cloning adds to this problem. In combination, these elements could seriously compromise the use of pigs as model for human diseases and the choice of breeds for this kind of work should be considered carefully. Further improvements in production of cloned/ transgenic embryos may ultimately reduce the incidence of malformations

Breed and number of born piglets and mortality < D 28	Skelet-al + mus-cles-and diaphrag ma	Urinary tract	Macro glossia	Heart	Go nades	Brain and spinal cord	Liver and gall bladder	Intes tine and pancre-as	Se-veral mal-formatio ns
All n = 289 59%	9	7	4	10	26	5	26	9	5
LW n = 117 50%	3	1	4	2	2	1			2
Gøttingen n = 98 63%	5	1		1	17	1	22	4	3
Yucatan n = 72 68%	1	5		7	7	3	4	5	